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Deliberate Abuse of Diphenoxylate Hydrochloride, a Schedule V Narcotic

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DIPHENOXYLATE is a meperidine congener frequently prescribed in the treatment of diarrhea. The drug is available in both tablet and liquid form (Lomotil, Colonil); each tablet and each 5 ml dose of the liquid contains 2.5 mg of diphenoxylate hydrochloride and 0.025 mg of atropine sulfate. Diphenoxylate hydrochloride is a schedule V narcotic.¹

The chemical structure of diphenoxylate hydrochloride is similar to that of meperidine,² and the drug carries many of the risks and hazards characteristic of the opiates. Mild side effects include drowsiness, rash, dizziness, depression and nausea. Treatment of overdose or individual hypersensitivity reaction is similar to that for meperidine or morphine intoxication. Prolonged monitoring of the patient is essential because, although there might be an initial response to narcotic antagonists, life-threatening respiratory depression may occur as late as 30 hours following ingestion.² Several cases of accidental overdose in children have been reported.³

As with other opiates, the drug also has a potential for abuse. Though at therapeutic ranges (20 mg of diphenoxylate hydrochloride per day or less, in divided doses) opioid effects do not occur, doses of 40 to 60 mg at a time have been

shown capable of producing a morphine-like euphoria.⁴ Morphine-like addiction is also theoretically possible following prolonged use of the drug at high doses.

Recently, I encountered a case of deliberate abuse of diphenoxylate hydrochloride, and ordered a computer search of the literature for further information. Considering the frequency with which this drug is prescribed, its schedule V rating, and the great demand among abusers for its opiate congeners, it was surprising to discover that deliberate abuse of diphenoxylate hydrochloride for its subjective effects has never been reported in the literature.

Report of a Case

A 32-year-old man came to the psychiatric outpatient clinic with complaints of anxiety and depression over his inability to carry out his duties satisfactorily at work.

The patient had a long history of drug abuse, including the intravenous abuse of heroin, and at age 24 had been admitted to hospital for what he described as an inadvertent overdose. Following this experience he became "more cautious" in his use of drugs, resolved to stop using heroin; the patient broke all contact with the *street scene*, but continued to abuse pills, in particular barbiturates, as well as prescription opiates such as pentazocine and propoxyphene. In addition, the patient related that he had, over the past year, begun to abuse diphenoxylate hydrochloride, taking large doses of the drug intermittently, but never more than once or twice a week for periods of up to several weeks at a time.

The patient's first experience with the drug had been with a prescription given to his wife by her doctor as prophylaxis before an intended trip abroad. He had found the bottle of pills and, not being familiar with the drug, had looked it up in the *Physicians' Desk Reference*. He had learned that it was an opiate and, in large doses, could produce opiate-like effects. The patient enjoyed the sensation, and then began taking the drug regularly. He found that most physicians would issue a prescription for diphenoxylate hydrochloride with little question when he complained of diarrhea, even when he would specifically request the drug by name. On several occasions he informed the physician that he was about to embark on an extended trip abroad, and received large supplies of the drug. The patient would ordinarily take 60 to 100 tablets for the desired

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effect, which he described as a euphoria qualitatively similar to that produced by other orally taken opiates. Concomitant ingestion of alcohol or other drugs seemed to result in potentiation of the effects.

On one occasion the patient shared a quantity of the drug with a friend who reported experiencing a similar *high*. The patient did not report having been bothered by any adverse atropinic side-effects at his usual dosage. The largest single amount he ever took was about 140 tablets; at this dosage he did experience pronounced dryness of the mouth, and woke up the following morning with nausea and a severe headache. Though his euphoria at the higher dosage was significantly enhanced, the patient says he ordinarily restricts his dosage of the drug for several reasons: (1) He is afraid of damaging his gastrointestinal tract, (2) he conscientiously wishes to avoid addiction and (3) the cost of the drug, even when purchased at a pharmacy (as opposed to the *street price*), is fairly expensive.

Discussion

That this drug is abused is not either astonishing or remarkable; any medication—no matter how ostensibly innocuous—carries with it the potential for abuse. What is remarkable is the ease with which this drug, a narcotic, is obtained, and the apparent willingness of many physicians to issue prescriptions to a patient with little or no question.

Many physicians seem unaware either of the opioid pharmacological structure of diphenoxylate hydrochloride or of its consequent potential for abuse and dependency. An informal survey I conducted among physicians at two academic centers seems to confirm this. Of 20 physicians interviewed (all of whom stated they prescribed the drug “at least occasionally,” and some said they did so “often”) only six were aware of the pharmacological structure of the medication and of its potential for abuse. Ironically, in our case report the patient apparently had made more assiduous use of the *Physicians' Desk Reference*, for his own purposes than had the prescribing physician.

The absence of previous case reports is puzzling. The patient's statement regarding the enthusiastic reaction of his friend to the drug suggests that his experience is neither idiosyncratic nor unique, though the patient's lack of contact with the *street scene* renders him incapable of accurately

appraising the extent to which the drug is being abused. The relatively high cost of the medication, even when obtained through licit channels, as well as the fact that diphenoxylate hydrochloride even as a salt is virtually insoluble in water⁵ and therefore cannot be abused parenterally, may be contributory. This by no means, however, obviates the possibility that deliberate abuse of the drug, though hitherto unreported, may be widespread. At present I am collecting and documenting a more extensive series of cases.

It has been stated that subtherapeutic amounts of atropine sulfate have been added to the compound to discourage deliberate overdose² (p 1449). This contention seems to conflict, however, with experimental data. Doses of less than 2 mg of atropine are, in an adult, unlikely to produce any clinically significant dysphoric effects.⁶ Therefore, even 60 tablets, which is a quantity significantly beyond that which is theoretically required to produce a morphine-like euphoria, would not contain a sufficient amount of atropine sulfate to disturb the patient sufficiently, presumably, to discourage deliberate overdose. This is particularly true because many opiate abusers are characteristically willing to tolerate considerable amounts of distress to obtain their high, “paying the price” not only in physical discomfort, but often, ultimately, in the typical, erosive, downward-spiral of the addicts' life-style.

The case reported here raises a number of questions. Clearly, there is a need for a heightened level of awareness among physicians concerning the pharmacological nature of the substance and its potential hazards, including the possibility of deliberate abuse and of habituation. Certainly a greater index of suspicion should be exercised when prescribing this medication for patients with histories of drug abuse, those who specifically request the drug by name and especially those patients who express a desire for inordinately large quantities of the medication. In addition, one must question the clinical sagacity of prescribing a narcotic-containing compound for any patient with diarrhea before potentially less hazardous drugs have been given an adequate trial. There is, unquestionably, no paucity of nonnarcotic medications, many of proven efficacy as well as safety, available on the market today.

Summary

Diphenoxylate hydrochloride is a drug frequently prescribed in the treatment of diarrhea.

Though it is chemically related to meperidine, deliberate abuse or dependency on this drug has never been reported. A case is presented in which the patient had been using the drug regularly, in large doses, for its morphine-like euphoriant effects. He had been obtaining the drug easily from physicians, and a heightened level of awareness among doctors concerning the abuse potential of this drug should result in greater vigilance in prescribing it.

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Epiglottitis in an Immunosuppressed Host

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EPIGLOTTITIS is an acute infection of the supraglottic larynx with a major risk of airway obstruction secondary to cellulitis and edema. Diagnosis is made by history and examination of the epiglottis by lateral neck x-ray study or, preferably, indirect mirror examination. Treatment consists of maintaining an airway, and administration of antibiotics, oxygenated mist and probably corticosteroids. This case presented unique therapeutic problems because of the underlying malignancy, impaired immune status, previous therapy and essentially irreversible coagulopathy.

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Report of a Case

In a 16-year-old girl with stage IV non-Hodgkin lymphoma in relapse despite multiple chemotherapy regimens, increasing sore throat, fever and dysphagia developed. The patient was admitted to hospital. After specimens for culture were obtained, treatment was started with cephalothin, gentamicin and carbenicillin because of the compromised immune status and possible sepsis.

Initial examination showed mild pharyngeal inflammation and enlarged, tender cervical nodes. Blood and urine cultures showed no growth and a throat culture showed normal flora and *Candida albicans*. A complete blood count at admission showed 600 leukocytes, a hematocrit reading of 22 percent and a platelet count of 13,000, with bleeding noted from venipuncture sites and the nose. After six units of platelet transfusion, the platelet count was 20,000, with continued bleeding.

Because a throat culture showed *Candida*, amphotericin was added to the regimen on the second hospital day. At this time the sore throat and dysphagia were worse, the patient was unable to swallow her saliva and mild airway obstruction was present. A lateral neck roentgenogram (Figure 1) was obtained and showed a typical enlarged epiglottis consistent with epiglottitis. Otolaryngologic consultation was obtained and examination showed a pale, swollen epiglottis with edema compromising the supraglottic airway. It was felt that neither an atraumatically placed endotracheal tube nor the most meticulous tracheostomy was a safe procedure because of thrombocytopenia refractory to treatment associated with bleeding. It was elected to begin administration of corticosteroids, 12 mg of dexamethasone (Decadron) given intravenously, followed by 4 mg every six hours. Within 12 hours the patient's condition was improved, and she was able to swallow her own saliva and some liquids. Eighteen hours later a repeat lateral neck roentgenogram showed no abnormalities (Figure 2). Two days later the patient had resumed a regular diet and the epiglottis was found to be normal on examination. She was discharged home 11 days after admission without sequelae.

Discussion

Epiglottitis is traditionally classified as an infectious disease of the larynx, but because of its morbidity and mortality it would be better to